REMARKS

In response to the Office Action dated August 7, 2009, Applicants have amended claims 133, 136, 137, and 140 solely to clarify particular aspects of the invention. No claims have been canceled and no new claims have been added. Support for the amendments may be found throughout the specification and original claims as filed, for example, on page 255, line 9 and page 261, lines 13-18. No new matter has been added. The above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Following the amendments, claims 133, and 136-143 are pending and under examination. Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks.

CLAIM AMENDMENTS

Applicants, without acquiescence and solely in a good faith effort to expedite prosecution, have amended claim 133 to recite a cell that is immobilized to a support by a composition comprising a salt and a 29 kDa fragment of fibronectin. Support for the amendments may be found throughout the specification and original claims as filed, for example, on page 255, line 9 and page 225, lines 13-18. No new matter has been added.

CLAIM OBJECTIONS

Claim 133 is objected to because of the following informalities: in step e), the term "environment" is misspelled and in step f), the term "data" should be inserted after the first occurrence of the term "experimental." Applicants respectfully submit that claim 133 has been amended to correctly spell the term "environment" and to insert the term "data" after the term "experimental." Thus, this basis of objection has been obviated. Reconsideration and withdrawal of this basis for objection is respectfully requested.

CLAIMS REJECTIONS UNDER 35 U.S.C. §103(A)

Claim 133 stands rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Rine *et al.* (WO98/06874) in view of Hashino *et al.* (J. Biochemistry, Vol. 122, pages 490-493(1997)) and Maxwell *et al.* (DNA Vol. 7, pages 557-562 (1988)). Specifically, the Action alleges that Rine *et al.* teach a process and apparatus that collects and stores data from a plurality of cells, said data being reporter signals generated as a response to a stimulation. The Action correctly notes that Rine *et al.* fail to teach or suggest recording the cell type, stimulus, cell culture medium, a time course of response, or a cell that is immobilized to a substrate by an actin-like compound. However, the Action alleges that Hashino *et al.* teach that fibronectin coated substrates improve the expression of electroporated polynucleotides in cells. Further, the Action alleges that Maxwell *et al.* teach that transient expression of electroporation expression vectors varies over time depending on the cell type transfected. Therefore, the Action concludes that it would have been obvious for the skilled artisan to combine the teachings of Rine *et al.*, Hashino *et al.*, and Maxwell *et al.* and arrive at the presently claimed invention.

Claims 136, 137, 140, and 141 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Rine *et al.* in view of Hashino *et al.* and Maxwell *et al.* and in further view of Rosenblum (U.S. Patent Application Publication No. 2002/0055935). Specifically, the Action alleges that Rine *et al.*, Hashino *et al.*, and Maxwell *et al.* are applied as noted above in the preceding obviousness rejection. The Action correctly notes that Rine *et al.*, Hashino *et al.*, and Maxwell *et al.* collectively fail to teach or suggest a comparison initiated by a requester, provision of the results of the comparison to the requester, or requesting of a comparison via the Internet. However, the Action contends that Rosenblum teaches a comparison initiated by a requester, provision of the results of the comparison to the requester, and requesting a comparison via the Internet. Therefore, the Action concludes that it would have been obvious to the skilled artisan to modify the process and apparatus of Rine *et al.* by the use of the biological database query method and apparatus of Rosenblum.

Claims 138, 139, 140, 142, and 143 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Rine *et al.* in view of Hashino *et al.*, Maxwell *et al.*, and Rosenblum, and in further view of Bimson *et al.* (U.S. Patent Application Publication No. 2001/0034748). Specifically, the Action alleges that Rine *et al.*, Hashino *et al.*, Maxwell *et al.*, and Rosenblum are applied as explained in the preceding obviousness rejection. The Action correctly notes that Rine *et al.*, Hashino *et al.*, Maxwell *et al.*, and Rosenblum collectively fail to teach or suggest providing the result of a search to the service requestor using a format in the extensible markup language (XML). However, the Action alleges that Bimson *et al.*, teach a process of searching a database and providing the results of the search in XML format. Therefore, the Action concludes that it would have been obvious for the skilled artisan to use XML format to output the search results of Rine *et al.* in view of Rosenblum.

Applicants respectfully traverse these bases for rejection.

Applicants respectfully submit that the Action fails to provide a sufficient basis for one having ordinary skill in the art to predictably arrive at the presently claimed invention with any reasonable expectation of success, and thus, the Action fails to establish a *prima facie* case of obviousness against the presently claimed invention. Moreover, the Action fails to establish a *prima facie* case of obviousness against the presently claimed invention because the references do not teach or suggest each and every element of the claims

At a minimum, it must be demonstrated that the cited references provide a sufficient basis to predictably arrive at the presently claimed invention, and even assuming, *arguendo*, that the cited references teach each claim feature, the Examiner must provide an explicit, apparent reason to combine these features in the fashion claimed by the Applicant with a reasonable expectation of success. See *KSR v. Teleflex,* Inc., No. 04-1350 at 4, 14 (U.S. Apr. 30, 2007) ("A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art").

In the instant case, the Action has failed to account for an apparatus for producing a digital cell comprising a cell immobilized to a support by a composition comprising a salt and a 29 kDa fragment of fibronectin, as presently claimed. Thus, the Action fails to provide sufficient

rationale for the skilled artisan to arrive at the presently claimed invention with any reasonable expectation of success.

Applicants respectfully submit that an important feature of the subject application is related to the Inventors' surprising and unexpected discovery that immobilizing the cells onto a specific substrate using a composition that comprises a salt, and a 29 kDa fragment of fibronectin, allows the claimed apparatus to be used efficiently to produce the digital cell.

Applicants further submit that it is clear from the as-filed specification and the art, that as of the priority date of the subject application it was not possible to effectively create a digital cell due to the fact that it was not possible to maintain a plurality of cells under a constant environment, which thus rendered the experimental conditions, such as transfection, unreliable (See, for example, page 243, line 29 to page 244, line 1 of the as-filed specification). In this regard, the unreliable experimental conditions resulted in a lack of significance between accumulated results of different experiments (See, for example, page 244, lines 2-3 of the specification as filed).

Moreover, while array technologies have been known since the priority date of the subject application, especially in the field of drug screening (See, for example, page 5, lines 6-22 of the specification as filed), no technique had been provided wherein the information about a particular cell could be provided with any reliable degree of accuracy (See, for example, page 5, lines 24-30 of the specification as filed).

Thus, one having ordinary skill in the art would appreciate that the presently claimed invention, which comprises the immobilization of cells onto a specific substrate using a composition that comprises a salt, and a 29 kDa fragment of fibronectin, provides an advantageous apparatus that can be effectively used to produce a digital cell (e.g., claim 133). Applicants respectfully submit the as-filed specification discloses that using the 29 kDa fibronectin fragment as a solid support during creating data for a digital cell surprisingly and unexpectedly increased the transfection efficiency to a reliable level **and** at the same time, significantly reduced the level of contamination. For example, page 161 of the as-filed specification recites:

> "Figures 2 and 3 show transfection efficiency when fibronectin fragments were used. Figure 4 shows the summary of the results. 29 kDa and 72

> kDa fragments exhibited a significant level of transfection activity, while a 43 kDa fragment had activity but its level was low. Therefore, it was suggested that an amino acid sequence contained in the 29 kDa fragment played a role in an increase in transfection efficiency. Substantially no contamination was found in the case of the 29 kDa fragment, while contamination was observed in the case of the other two fragments (43 kDa and 72 kDa)."

In contrast, the art cited in the Action collectively fails to teach or suggest an apparatus for producing a digital cell comprising a cell immobilized to a support by a composition comprising a salt and a 29 kDa fragment of fibronectin, as presently claimed

The Action alleges that Hashino *et al.* show that fibronectin coated substrates improve the expression of **electroporated** expression vectors. Applicants respectfully disagree. Applicants respectfully submit that the presently claimed invention uses solid phase transfection, and thus, the skilled artisan would not look to Hashino *et al.* because they are concerned with increasing the survivability of **electroporated** cells (see, for example, Example 2, and Figures 13A, 13C, and 14B of the as-filed specification). Applicants respectfully submit that Hashino teach that survival of **electroporated** cells increases when cultured on fibronectin because fibronectin increases the recovery of cells damaged by an electric pulse (see page 491, 2nd column of Hashino *et al.*). Hashino *et al.* state that "[c]ultivation of cells on a substrate precoated with fibronectin fragments enhanced the wound healing of the damaged cells, causing the recovery of the cells transfected with DNA which can not survive on non-coated dishes due to the damage by **electroporation**." See page 492, first column. Moreover, Applicants respectfully submit that Hashino *et al.* are completely silent with regard to using a 29 kDa fibronectin fragment, which has the unexpected properties of increasing transfection efficiency **and** decreasing contamination. Further, the skilled artisan would not extrapolate the findings of using fibronectin to enhance the repair of electroporated cells with use of the 29 kDa fibronectin fragment in a digital cell for increasing transfection efficiency and decreasing contamination as presently claimed. Accordingly, in view of Hashino *et al.*, one having skill in the art would not have a reasonable expectation of success in arriving at the presently claimed invention, wherein the cell is immobilized to a support by a composition comprising a salt and a 29 kDa fragment of fibronectin.

Applicants respectfully submit that Hashino *et al.* fail to remedy the insufficiencies of Rine *et al.*; thus, Rine *et al.* and Hashino *et al.* collectively fail to establish a *prima facie* case of obviousness against the presently claimed invention.

The Action also concludes that it would have been obvious to measure a time course of reporter gene expression subsequent to electroporation because Maxwell *et al.* shows that transient reporter gene expression from an expression vector peaks at a time subsequent to electroporation, and that the time of maximum expression must be empirically determined for the cell line that is being studied. Applicants respectfully disagree.

As noted above, the presently claimed invention is directed to an apparatus that uses a solid phase transfection. Thus, the skilled artisan would not consider nor rely on Maxwell *et al.* because Maxwell *et al.* explicitly teach empirically determining the time-course of transgene expression in electroporated cells. Accordingly, in view of Maxwell *et al.*, one having skill in the art would not have a reasonable expectation of success in arriving at the presently claimed invention, which comprises steps of recording the cell type, stimulus, cell culture medium, and a time course of response. Applicants respectfully submit Maxwell *et al.* also fail to teach, suggest or provide any rationale for the immobilization of cells to a support using a composition comprising a salt and a 29 kDa fragment of fibronectin. Thus, Maxwell *et al.* fail to remedy the insufficiencies of Hashino *et al.* and Rine *et al.*; thus, Rine *et al.,* Maxwell *et al.*, and Hashino *et al.* collectively fail to establish a *prima facie* case of obviousness against the presently claimed invention.

In regard to the rejection of claims 136, 137, 140, and 141 over Rine *et al.* in view of Hashino *et al.*, Maxwell *et al.*, and Rosenblum, the Action concludes that it would have been obvious to the skilled artisan to modify the process and apparatus of Rine *et al.* by the use of the biological database query method and apparatus of Rosenblum, because Rosenblum shows how access to biological databases by requester may be performed conveniently via the Internet. Applicants respectfully disagree and submit that even if the skilled artisan would combine the references as suggested by the Examiner, he would have no reasonable expectation of success in arriving at the presently claimed invention. Applicants respectfully submit that Rosenblum fails to teach, suggest or provide any rationale for the immobilization of cells to a support using a

composition comprising a salt and a 29 kDa fragment of fibronectin. Thus, Rosenblum fails to remedy the insufficiencies of Rine *et al.*, Hashino *et al.*, and Maxwell et al; thus, these references collectively fail to establish a *prima facie* case of obviousness against the presently claimed invention.

In regard to the rejection of claims 138, 139, 140, 142, and 143 over Rine *et al.* in view of Hashino *et al.*, Maxwell *et al.*, Rosenblum, and Bimson *et al.*, the Action concludes that it would have been obvious to the skilled artisan to use XML format to output the search results of Rine *et al.*, because Bimson *et al.* teach the use of XML formats as a known and useful format for search results. Applicants respectfully disagree and submit that even if the skilled artisan would combine the references as suggested by the Examiner, he would have no reasonable expectation of success in arriving at the presently claimed invention. Applicants respectfully submit Bimson *et al.* fail to teach, suggest or provide any rationale for the immobilization of cells to a support using a composition comprising a salt and a 29 kDa fragment of fibronectin. Thus, Bimson *et al.* fail to remedy the insufficiencies of Rine *et al.*, Hashino *et al.*, Maxwell et al, and Rosenblum; thus, these references collectively fail to establish a *prima facie* case of obviousness against the presently claimed invention.

Applicants respectfully submit that the references cited in the Action fail to disclose or provide any rationale any type of apparatus, support, or composition comprising a cell that is immobilized to a composition comprising a salt and a 29 kDa fragment of fibronectin. Accordingly, even if the references were combined in the manner suggested in the Action, the skilled artisan would not have a reasonable expectation of success of practicing the presently claimed invention; especially in view of the surprising and unexpected increase in transfection efficiency and decrease in contamination afforded by the use of the 29 kDa fibronectin fragment as presently claimed.

Applicants respectfully submit that the Action fails to establish a *prima facie* case of obviousness against the presently claimed invention. Reconsideration and withdrawal of these bases for rejection is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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